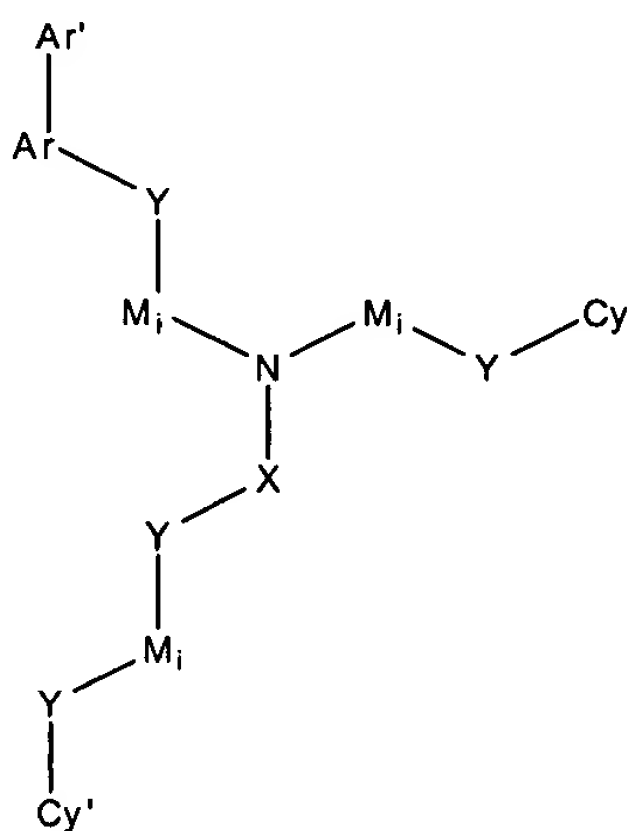


In the claims:

1. **(Previously presented)** A method of increasing expression of vascular endothelial growth factor (VEGF) in a subject with ischemic myocardial tissue, wherein the method comprises administering to a subject in need thereof an effective amount of a hedgehog agonist, wherein the hedgehog agonist is a small organic molecule represented by the general formula (XII):

Formula XII



wherein, as valence and stability permit,

Ar and Ar' independently represent substituted or unsubstituted aryl or heteroaryl rings;

Y, independently for each occurrence, is absent or represent -N(R)-, -O-, -S-, or -Se-;

X is selected from -C(=O)-, -C(=S)-, -S(O<sub>2</sub>)-, -S(O)-, -C(=NCN)-, -P(=O)(OR<sub>2</sub>)-, and a methylene group optionally substituted with 1-2 groups such as lower alkyl, alkenyl, or alkynyl groups;

M represents, independently for each occurrence, a substituted or unsubstituted methylene group, or two M taken together represent substituted or unsubstituted ethene or ethyne;

R represents, independently for each occurrence, H or substituted or unsubstituted aryl, heterocyclyl, heteroaryl, aralkyl, heteroaralkyl, alkynyl, alkenyl, or alkyl, or two R taken together may form a 4- to 8-membered ring;

Cy and Cy' independently represent substituted or unsubstituted aryl, heterocyclyl, heteroaryl, or cycloalkyl, including polycyclic groups;

i represents, independently for each occurrence, an integer from 0 to 5; and

n, individually for each occurrence, represents an integer from 0 to 10;

or a pharmaceutically acceptable salt thereof.

2. **(Previously presented)** The method of claim 1, wherein the step of administering comprises contacting the hedgehog agonist with a mesenchymal cell of the subject.

3-25. **(Cancelled)**

26. **(Previously presented)** The method of claim 1, wherein the hedgehog agonist has a molecular weight less than 750 amu.

27-36. **(Cancelled)**

37. **(Previously presented)** The method of claim 1, wherein said small organic molecule agonizes hedgehog signal transduction via an interaction with any of *hedgehog*, *patched*, *gli*, or *smoothened*.

38. **(Previously presented)** The method of claim 1, wherein said small organic molecule agonizes hedgehog signal transduction via an interaction with *smoothened*.

39. **(Previously presented)** The method of claim 1, wherein administering the hedgehog agonist comprises direct injection to ischemic myocardium.

40. **(Previously presented)** The method of claim 1, wherein administering the hedgehog agonist comprises intrapericardial administration.

41. **(Previously presented)** The method of claim 1, wherein the hedgehog agonist is administered by intracoronary catheter delivery.

42. **(Previously presented)** The method of claim 1, wherein the hedgehog agonist is administered systemically.
43. **(Previously presented)** The method of claim 1, wherein at least one of Ar and Ar' is a phenyl ring.
44. **(Previously presented)** The method of claim 1, wherein at least one of Ar and Ar' is a heteroaryl ring,
45. **(Previously presented)** The method of claim 44, wherein the heteroaryl ring is selected from pyridyl, thiazolyl, thienyl, or pyrimidyl.
46. **(Previously presented)** The method of claim 1, wherein Y is absent from all positions.
47. **(Previously presented)** The method of claim 1, wherein Cy' is a substituted or unsubstituted aryl or heteroaryl.
48. **(Previously presented)** The method of claim 47, wherein Cy' is a substituted or unsubstituted bicyclic or heteroaryl ring.
49. **(Previously presented)** The method of claim 48, wherein the substituted or unsubstituted bicyclic or heteroaryl ring is benzothiophene.
50. **(Previously presented)** The method of claim 1, wherein X is -C(=O)-.
51. **(Previously presented)** The method of claim 1, wherein Cy represents a substituted or unsubstituted non-aromatic carbocyclic or heterocyclic ring.
52. **(Previously presented)** The method of claim 1, wherein Cy includes an amine within the atoms of the ring or on a substituent of the ring.

53. **(Previously presented)** The method of 1, wherein Cy is selected from pyridyl, imidazolyl, pyrrolyl, piperidyl, pyrrolidyl, piperazyl, and/or bears an amino substituent.

54. **(Previously presented)** The method of claim 53, wherein Cy is a 5- to 7-membered ring.

55. **(Previously presented)** The method of claim 54, wherein Cy is a six-membered ring directly attached to N and bears an amino substituent at the 4 position of the ring relative to N.

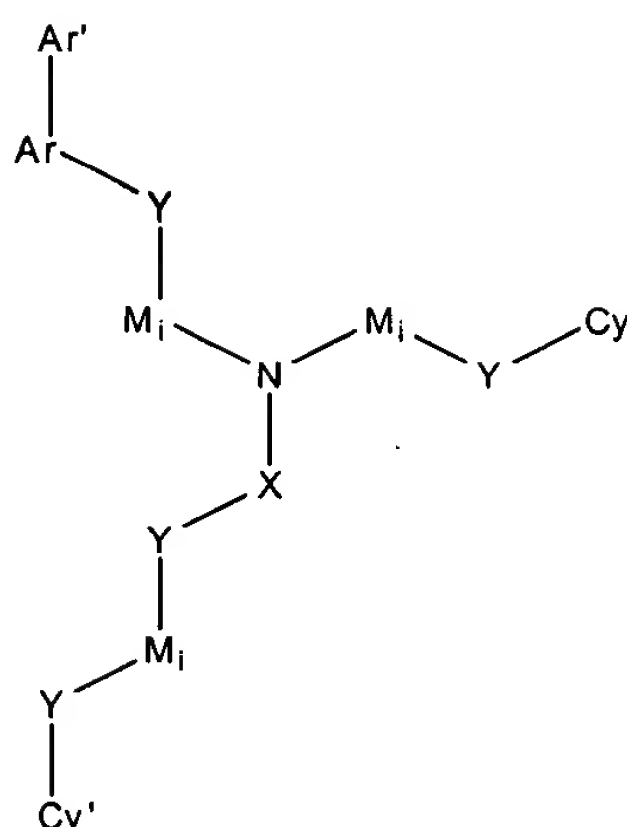
56. **(Previously presented)** The method of claim 55, wherein the N and amine substituents are disposed *trans* on the ring.

57. **(Previously presented)** The method of claim 1, wherein substituents on Ar and Ar' are selected from halogen, lower alkyl, lower alkenyl, aryl, heteroaryl, carbonyl, thiocarbonyl, ketone, aldehyde, amino, acylamino, cyano, nitro, hydroxyl, azido, sulfonyl, sulfoxido, sulfate, sulfonate, sulfamoyl, sulfonamido, phosphoryl, phosphonate, phosphinate,  $-(CH_2)_p$ alkyl,  $-(CH_2)_p$ alkenyl,  $-(CH_2)_p$ alkynyl,  $-(CH_2)_p$ aryl,  $-(CH_2)_p$ aralkyl,  $-(CH_2)_p$ OH,  $-(CH_2)_p$ O-lower alkyl,  $-(CH_2)_p$ O-lower alkenyl,  $-O(CH_2)_nR$ ,  $-(CH_2)_pSH$ ,  $-(CH_2)_pS$ -lower alkyl,  $-(CH_2)_pS$ -lower alkenyl,  $-S(CH_2)_nR$ ,  $-(CH_2)_pN(R)_2$ ,  $-(CH_2)_pNR$ -lower alkyl,  $-(CH_2)_pNR$ -lower alkenyl,  $-NR(CH_2)_nR$ , and protected forms of the above, wherein p, individually for each occurrence, represents an integer from 0 to 10, preferably from 0 to 5.

58. **(Previously presented)** A method of increasing expression of vascular endothelial growth factor (VEGF) in a subject with ischemic myocardial tissue, comprising administering to a subject in need thereof an effective amount of means for promoting hedgehog signaling.

59. **(New)** A method for improving myocardial function following myocardial ischemia, comprising systemically administering to a subject in need thereof an effective amount of a hedgehog agonist, wherein the hedgehog agonist is a small organic molecule represented by the general formula (XII):

Formula XII



wherein, as valence and stability permit,

Ar and Ar' independently represent substituted or unsubstituted aryl or heteroaryl rings;

Y, independently for each occurrence, is absent or represent -N(R)-, -O-, -S-, or -Se-;

X is selected from -C(=O)-, -C(=S)-, -S(O<sub>2</sub>)-, -S(O)-, -C(=NCN)-, -P(=O)(OR<sub>2</sub>)-, and a methylene group optionally substituted with 1-2 groups such as lower alkyl, alkenyl, or alkynyl groups;

M represents, independently for each occurrence, a substituted or unsubstituted methylene group, or two M taken together represent substituted or unsubstituted ethene or ethyne;

R represents, independently for each occurrence, H or substituted or unsubstituted aryl, heterocyclyl, heteroaryl, aralkyl, heteroaralkyl, alkynyl, alkenyl, or alkyl, or two R taken together may form a 4- to 8-membered ring;

Cy and Cy' independently represent substituted or unsubstituted aryl, heterocyclyl, heteroaryl, or cycloalkyl, including polycyclic groups;

i represents, independently for each occurrence, an integer from 0 to 5; and

n, individually for each occurrence, represents an integer from 0 to 10;

or a pharmaceutically acceptable salt thereof.

60. (New) The method of claim 59, wherein at least one of Ar and Ar' is a phenyl ring.

61. (New) The method of claim 59, wherein at least one of Ar and Ar' is a heteroaryl ring,

62. (New) The method of claim 61, wherein the heteroaryl ring is selected from pyridyl, thiazolyl, thienyl, or pyrimidyl.
63. (New) The method of claim 59, wherein Y is absent from all positions.
64. (New) The method of claim 59, wherein Cy' is a substituted or unsubstituted aryl or heteroaryl.
65. (New) The method of claim 64, wherein Cy' is a substituted or unsubstituted bicyclic or heteroaryl ring.
66. (New) The method of claim 65, wherein the substituted or unsubstituted bicyclic or heteroaryl ring is benzothiophene.
67. (New) The method of claim 59, wherein X is -C(=O)-.
68. (New) The method of claim 59, wherein Cy represents a substituted or unsubstituted non-aromatic carbocyclic or heterocyclic ring.
69. (New) The method of claim 59, wherein Cy includes an amine within the atoms of the ring or on a substituent of the ring.
70. (New) The method of 59, wherein Cy is selected from pyridyl, imidazolyl, pyrrolyl, piperidyl, pyrrolidyl, piperazyl, and/or bears an amino substituent.
71. (New) The method of claim 70, wherein Cy is a 5- to 7-membered ring.
72. (New) The method of claim 71, wherein Cy is a six-membered ring directly attached to N and bears an amino substituent at the 4 position of the ring relative to N.

73. (New) The method of claim 72, wherein the N and amine substituents are disposed *trans* on the ring.

74. (New) The method of claim 59, wherein substituents on Ar and Ar' are selected from halogen, lower alkyl, lower alkenyl, aryl, heteroaryl, carbonyl, thiocarbonyl, ketone, aldehyde, amino, acylamino, cyano, nitro, hydroxyl, azido, sulfonyl, sulfoxido, sulfate, sulfonate, sulfamoyl, sulfonamido, phosphoryl, phosphonate, phosphinate,  $-(CH_2)_p$ alkyl,  $-(CH_2)_p$ alkenyl,  $-(CH_2)_p$ alkynyl,  $-(CH_2)_p$ aryl,  $-(CH_2)_p$ aralkyl,  $-(CH_2)_pOH$ ,  $-(CH_2)_pO$ -lower alkyl,  $-(CH_2)_pO$ -lower alkenyl,  $-O(CH_2)_nR$ ,  $-(CH_2)_pSH$ ,  $-(CH_2)_pS$ -lower alkyl,  $-(CH_2)_pS$ -lower alkenyl,  $-S(CH_2)_nR$ ,  $-(CH_2)_pN(R)_2$ ,  $-(CH_2)_pNR$ -lower alkyl,  $-(CH_2)_pNR$ -lower alkenyl,  $-NR(CH_2)_nR$ , and protected forms of the above, wherein p, individually for each occurrence, represents an integer from 0 to 10, preferably from 0 to 5.